

At page ~~11~~, line 9, after "peptides of the invention", please insert -- (SEQ ID NO:2) --.

In Figure ~~16~~, please replace "pNP2203" with --pNP2204--.

Before the first sentence of the specification, please insert:

A2
00397201.1
~~4-~~ This is a continuation of U.S. Application Serial No. 08/913,362, filed November 13, 1997, which is the National Stage of International Application No. PCT/CA96/00157, filed March 15, 1996, which claims the benefit of U.S. Provisional Application Serial No. 60/001,983, filed August 4, 1995, and which claims the benefit of U.S. Application Serial No. 08/406,362, filed March 17, 1995, now abandoned.

IN THE CLAIMS

Please cancel all pending claims 1-90 without prejudice or disclaimer, and insert new claims 91-169:

Sub C12
A3
cm. x
new DNA seq.
no
-- 91. An isolated polynucleotide that hybridizes under stringent conditions to either (a) a DNA sequence encoding a *Neisseria*-surface protein or (b) the complement of a DNA sequence encoding a *Neisseria* surface protein, wherein said *Neisseria* surface protein:

- (i) is resistant to proteinase K, and
- (ii) has an apparent molecular weight of 22 kDa.

92. The polynucleotide of claim 91, wherein said *Neisseria* surface protein is encoded by a DNA molecule that comprises bases 200 to 667 of SEQ ID NO:1.

93. The polynucleotide of claim 92, wherein said DNA molecule comprises bases 143 to 667 of SEQ ID NO:1.
94. The polynucleotide of claim 93, wherein said DNA molecule comprises SEQ ID NO:1.
-
95. The polynucleotide of claim 91, wherein said *Neisseria* surface protein is encoded by a DNA molecule that comprises bases 173 to 643 of SEQ ID NO:3.
96. The polynucleotide of claim 95, wherein said DNA molecule comprises bases 116 to 643 of SEQ ID NO:3.
97. The polynucleotide of claim 96, wherein said DNA molecule comprises SEQ ID NO:3.
-
98. The polynucleotide of claim 91, wherein said *Neisseria* surface protein is encoded by a DNA molecule that comprises bases 265 to 732 of SEQ ID NO:5.
99. The polynucleotide of claim 98, wherein said DNA molecule comprises bases 208 to 732 of SEQ ID NO:5.
100. The polynucleotide of claim 99, wherein said DNA molecule comprises SEQ ID NO:5.
-
101. The polynucleotide of claim 91, wherein said *Neisseria* surface protein is encoded by a DNA molecule that comprises 298 to 765 of SEQ ID NO:7.
102. The polynucleotide of claim 101, wherein said DNA molecule comprises 241 to 765 of SEQ ID NO:7.

103. The polynucleotide of claim 102, wherein said DNA molecule comprises SEQ ID NO:7.
104. An isolated polynucleotide comprising bases 200 to 667 of SEQ ID NO:1.
105. The isolated polynucleotide according to claim 104, comprising bases 143 to 667 of SEQ ID NO:1.
106. The isolated polynucleotide according to claim 105, comprising SEQ ID NO:1.
107. An isolated polynucleotide comprising bases 173 to 643 of SEQ ID NO:3.
108. The isolated polynucleotide according to claim 107, comprising bases 116 to 643 of SEQ ID NO:3.
109. The isolated polynucleotide according to claim 108, comprising SEQ ID NO:3.
110. An isolated polynucleotide comprising bases 265 to 732 of SEQ ID NO:5.
111. The isolated polynucleotide according to claim 110, comprising bases 208 to 732 of SEQ ID NO:5.
112. The isolated polynucleotide according to claim 111, comprising SEQ ID NO:5.
113. An isolated polynucleotide comprising bases 298 to 765 of SEQ ID NO:7.
114. The isolated polynucleotide according to claim 113, comprising bases 241 to 765 of SEQ ID NO:7.

115. The isolated polynucleotide according to claim 114, comprising SEQ ID NO:7.

116. A recombinant DNA molecule, comprising (i) a polynucleotide that hybridizes under stringent conditions to said complement of claim 91 and (ii) an expression control sequence operatively linked to said polynucleotide.

117. The recombinant DNA molecule of claim 116, wherein said expression control sequence comprises an inducible expression control sequence.

118. The recombinant DNA molecule of claim 117, wherein said inducible expression control sequence is inducible by a stimulus selected from the group consisting of temperature, lactose, and IPTG.

119. The recombinant DNA molecule of claim 117, wherein said inducible expression control sequence is selected from the group consisting of λ PL, λ PR, TAC, T7, T3, LAC, and TRP promoters.

120. The recombinant DNA molecule of claim 116, wherein said DNA molecule is selected from the group consisting of pNP2202, pNP2203, and pNP2204.

121. A unicellular host transformed with the recombinant DNA molecule of claim 116.

122. The unicellular host of claim 121, wherein said host is selected from the group consisting of strains of *E.coli* JM109, *E.coli* BL21 (DE3), *E.coli* DH5 α F'IQ, *E.coli* W3110, *E.coli* JM105, *E.coli* BL21, *E.coli* TOPP1, *E.coli* TOPP2, and *E.coli* TOPP3.

Sub C:7
123. A method for producing the polynucleotide of claim 91, comprising the steps of culturing the unicellular host of claim 121 and isolating said polynucleotide.

~~124. An isolated polypeptide encoded by a polynucleotide that hybridizes under stringent conditions to the complement of a DNA sequence encoding a *Neisseria* surface protein, wherein said *Neisseria* surface protein:~~

- ~~(i) is resistant to proteinase K, and
(ii) has an apparent molecular weight of 22 kDa,
wherein said polypeptide is antigenic.~~

125. The isolated polypeptide of claim 124, comprising a sequence selected from the group of sequences consisting of SEQ ID NO:2; SEQ ID NO:4; SEQ ID NO:6; and SEQ ID NO:8.

126. The isolated polypeptide of claim 124, comprising a sequence selected from the group of sequences consisting of SEQ ID NO:9; SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, and SEQ ID NO:26.

127. The isolated polypeptide of claim 124, comprising amino acids 31 to 55 of SEQ ID NO:2.

128. The isolated polypeptide of claim 124, comprising amino acids 51 to 86 of SEQ ID NO:2.

129. The isolated polypeptide of claim 124, comprising amino acids 110 to 140 of SEQ ID NO:2.

130. The isolated polypeptide of claim 124, wherein said polypeptide is free from other proteins of *Neisseria* origin.

131. A method of isolating the polypeptide of claim 124, comprising:

- isolating a culture of *Neisseria meningitidis* bacteria;
- isolating an outer membrane portion from said culture; and
- isolating said antigen from said outer membrane portion.

132. The method according to claim 131, further comprising treating said outer membrane with proteinase K.

133. A pharmaceutical composition comprising the polypeptide of claim 124.

134. The pharmaceutical composition of claim 133, which is a vaccine.

135. The pharmaceutical composition of claim 134, comprising a pharmaceutical excipient.

136. A method of preventing infection by a *Neisseria* pathogen, comprising administering an effective amount of the vaccine of claim 134.

137. The method according to claim 136, wherein said pathogen is a *Neisseria meningitidis*.

138. An antibody or a fragment thereof that specifically binds to the polypeptide of claim 124.

139. The antibody of claim 138, wherein said polypeptide is a *Neisseria* 22 kDa surface protein.

140. The antibody of claim 139, wherein said *Neisseria* 22 kDa surface protein is a *Neisseria meningitidis* 22 kDa surface protein.

141. The antibody of claim 138, which is a monoclonal antibody.

142. The antibody of claim 141, which is of murine origin.

143. The antibody of claim 142, which is an IgG isotype.

144. The antibody of claim 141, which is selected from the group consisting of Me-1, Me-2, Me-3, Me-5, Me-6, and Me-7.

145. A method for isolating the antibody of claim 138, comprising:
a) introducing a preparation of a *Neisseria* organism into a mammal; and
b) isolating a serum from the mammal containing said antibody.

146. The method according to claim 145, wherein said *Neisseria* organism is *Neisseria meningitidis*.

147. A method for isolating the monoclonal antibody of claim 141, comprising,
a) introducing a preparation of a *Neisseria* organism to antibody producing cells of a mammal;
b) fusing said cells with myeloma cells to form hybridoma cells; and
c) isolating said monoclonal antibody from said hybridoma cells.

148. The method according to claim 147, wherein said *Neisseria* organism is *Neisseria meningitidis*.

149. A pharmaceutical composition comprising the antibody or fragment thereof of claim 138.

150. The pharmaceutical composition of claim 149, which is a vaccine.

151. The pharmaceutical composition of claim 149, comprising a pharmaceutical excipient.

152. The pharmaceutical composition according to claim 149, wherein said antibody is selected from the group consisting of Me-1 and Me-7.

153. A method for treating a patient infected with a *Neisseria* pathogen, comprising administering an effective amount of any one of the pharmaceutical composition of claim 149.

154. The method according to claim 153, wherein said pathogen is *Neisseria meningitidis*.

155. A method for detection of a *Neisseria* antigen in a biological sample, comprising:

- a) isolating a biological sample from a patient;
- b) incubating the antibody of claim 138 with said biological sample; and
- c) detecting antibody specifically bound to the antigen.

156. The method according to claim 155, wherein said pathogen is a *Neisseria meningitidis*.

157. The method according to claim 155, wherein said antibody is selected from the group consisting of Me-1 and Me-7.

158. A method for detection of an antibody specific to a *Neisseria* antigen in a biological sample, comprising:

- a) isolating a biological sample from a patient;
- b) incubating the antigen of claim 124 with said the biological sample; and
- c) detecting antigen specifically bound to the antibody.

159. The method according to claim 158, wherein said antigen is a *Neisseria meningitidis* antigen.

160. The method according to claim 159, wherein said antigen is a *Neisseria meningitidis* 22 kDa surface protein.

161. A method for detection of a *Neisseria* pathogen in a patient, comprising:

- a) labeling the antibody of claim 138 with a detectable label;
- b) administering the labeled antibody to said patient; and
- c) detecting labeled antibody specifically bound to the pathogen.

162. The method according to claim 161, wherein said pathogen is *Neisseria meningitidis*.

163. A method for detection of *Neisseria* bacteria in a biological sample, comprising,

- a) isolating a biological sample from a patient;
- b) contacting said sample with a DNA probe that is capable of hybridizing under stringent conditions with a polynucleotide encoding a *Neisseria* surface protein according to claim 91; and
- c) detecting hybridization by said DNA probe to said polynucleotide.

- A3
Cm
002.397201.1
164. The method according to claim 163, wherein said DNA probe comprises the polynucleotide of claim 94.
165. The method according to claim 163, wherein said DNA probe comprises the polynucleotide of claim 97.
166. The method according to claim 163, wherein said DNA probe comprises the polynucleotide of claim 100.
167. The method according to claim 163, wherein said DNA probe comprises the polynucleotide of claim 103.
168. The method according to claim 163, wherein said DNA probe is an oligomer having a sequence complementary to at least 6 contiguous nucleotides of the polynucleotide of claim 91.
169. The method according to claim 163, further comprising a step of amplifying a target DNA by polymerase chain reaction with a set of oligomers having a sequence (i) complementary to at least 6 contiguous nucleotides of the polynucleotide of claim 91 and (ii) flanking said target DNA. - -
- Sub
G-1